REMARKS

Claims 30, 36 and 37 are under examination in this application; the remainder of the claims having been withdrawn from consideration. Claims 30, 36 and 37 are under examination with respect to the combination of species of perfluoropropane and human protein.

Double patenting

Applicant previously agreed to file an appropriate terminal disclaimer in this application in order to overcome the rejections based on double patenting. As discussed with Examiner Hollinden, this application contains only method-of-use claims whereas some of the cited patents contain claims of other types, namely composition and/or method-of-manufacture. The division of such claims among these patents was the result of requirements for restriction issued early in the prosecution of applications resulting in these patents. It was agreed therefore that in a method-of-use case such as the present it would be satisfactory for a terminal disclaimer to refer only to cited patents having method-of-use claims.

The cited U.S. patents 5,409,688, 5,573,751, 5,558,853 and 5,558,854 do not contain method-of-use claims. The terminal disclaimer, therefore, will be with respect to the remaining three U.S. patents, nos. 5,393,524, 5,558,094 and 5,558,855.

A double-patenting rejection was also issued with respect to a number of pending applications. All but one of these is still pending, so that Applicant submits that no terminal disclaimer is yet required in respect of those. To the contrary, terminal disclaimers may be necessary in those pending applications with respect to a patent that is issued in this application. One cited application, however, has issued as a patent. This is application No. 08 /770,522, which has become U.S. patent 6,156,292. It contains method-of-use claims, and therefore will be included in the terminal disclaimer.

Applicant submits that the terminal disclaimer as stated above will be satisfactory in this case and trusts the Examiner agrees. Should any other of the cited pending applications issue as

a patent that contains method-of-use claims, prior to the allowance of claims in this application, they will also be included.

Rejection under 35 U.S.C. 112

All rejections of claims over prior art have been overcome. There remains a rejection of claims 30, 36 and 37 under 35 U.S.C. 112 as lacking written description. Applicant respectfully submits that this rejection is not sustainable, particularly in view of the declarations previously filed in this application, and that this rejection should be withdrawn.

Applicant further submits that a rejection of claims as failing to meet the requirements of 35 U.S.C. based only on the elected species is inappropriate; furthermore, once the claims in this application have been examined and found allowable with respect to the elected species, the remainder of the claimed genus should be searched and examined.

First, declarations of Dr. Pamela Hilpert filed in this application clearly show that the concept under examination, the furnishing of ultrasound contrast agents containing perfluoropropane and human protein, would be viewed by those skilled in the art as being among the inventive concepts in the possession of the inventor when the application was filed.

The application is directed principally to the selection of perfluorocarbon gases for use as microbubbles for ultrasound contrast imaging. This is accomplished by determining a value, referred to as the Q value, for a proposed gas. This value is related to the solubility of the gas in water in comparison to that of air. The most suitable gases are said to be those with the highest q values.

As pointed out in Dr. Hilpert's Fourth declaration, dated April, 1999, perfluoropropane has the fifth highest Q value of the gases in Table II [par. 6(3)] and thus was clearly one of the gases preferred for use in ultrasound contrast agents.

The specification twice states (p. 20 lines 30-33 and p. 21 lines 15-17) that the products containing microbubbles can be produced using existing techniques for preparation of such products.

Thus it would be clear to one skilled in the art from reading the specification that the invention included ultrasound contrast agents of the general types already known but containing microbubbles of the gases selected as above.

The specification itself, in the sections entitled "The Materials Presently Used as Contrast-Enhancing Agents" (pp. 13-20) describes a few existing techniques for ultrasound contrast agents. Several of these involve the use of gaseous microbubbles, for instance:

- suspensions of crystals in a saccharide diluent which contain or generate microbubbles (p. 15 lines 1-12);
- aqueous suspensions of liposomes containing gases or gas precursors (p. 15 line 34 – page 16 line 14);
- liquids such as aqueous solutions of human protein, containing microbubbles (p. 17 lines 16-26; see also examples 1 and 5);
- microspheres containing microbubbles (p. 12, lines 19-23).

Compositions containing gaseous perfluoropropane microbubbles and human protein are thus one of only a few microbubble formulations specifically mentioned in this application.

Furthermore, as explained in the Hilpert declaration [paragraph 6, particularly 6(4) - 6(6)], protein-stabilized air microbubbles were well known in the art and were a commercial product at the time this application was filed. This, together with their being highlighted in the specification, provides the basis for Dr. Hilpert's statement that their use in combination with perfluoropropane was clearly disclosed in the application as an aspect of the inventive concept, and one skilled in the art would clearly recognize it as such.

The Examiner characterized the disclosure of human protein as "part of a large number of additional adjuvants which may be used". Applicant submits that this is an overstatement. The specification discloses about a half-dozen different known types of formulations

that employ microbubbles, of which claim 37 mentions four. This includes protein-containing formulations as well as the ones mentioned above. This is in no way a "large number".

The Examiner took the position that the Fourth Hilpert declaration "merely represents the opinion of Dr. Hilpert and does not provide any factual evidence" (citing the case of In re Payne). However, this assessment of Dr. Hilpert's declarations is not in accord with the law.

The Examiner's position is practically identical to the position taken by the examiner (and found by the CAFC to be in error) in the case of In re Alton, 37 USPQ2d 1578 (Fed. Cir. 1996). In that case, as here, the applicant submitted a declaration providing specific reasons why those skilled in the art would have understood, from the specification, that the applicant was in possession of the claimed invention. The CAFC stated (p. 1583): "[T]he declaration is offering factual evidence in an attempt to explain why (emphasis in original) one of ordinary skill in the art would have understood the specification to describe [the claimed invention]", and characterized the declaration as one of fact, not opinion.

The opinion sums up the point at page 584:

> "The Wall declaration addresses why the claimed subject matter, although not identical to the analog described in the specification, was in Alton's possession. The statement in the examiner's answer that the number of possible analogs encompassed by the specification is substantial does not rebut the thrust of the Wall declaration because the Wall declaration explains why one of ordinary skill in the art would have realized that Alton had possession of one particular analog. ...
>
> First, by concluding that the Wall declaration addressed an issue of law instead of an issue of fact, and second, by failing to articulate adequate reasons to rebut the Wall declaration, the examiner and the Board failed to consider the totality of the record for the purpose of issuing a final rejection and thus erred as a matter of law."

The Payne case is not relevant to this issue. It involved a declaration submitted in response to an obviousness rejection, and which failed to explain why results were unexpected.

The claims under consideration herein cover a combination of one of a small number of preferred gases with one of a small number of known techniques for producing microbubble compositions for use in ultrasound imaging. As shown in the declaration of Dr. Hilpert, those skilled in the art would recognize that the claims cover one of the types of compositions preferred by and in the possession of the inventor when the priority application was filed.

Applicant thus submits that the claims under examination meet the written description requirement of 35 U.S.C. 112.

Applicant further submits that a different procedure is to be followed at this point. The Examiner had required election among some subspecies embraced by a generic claim (Claim 30). The Examiner then properly examined claim 30 with respect to the elected species and eventually withdrew all rejections based on the prior art, with the exception of the double patenting rejections, for which Applicant offered to file the terminal disclaimer as discussed above. The Examiner should then have proceeded to examine the claims to their full extent, i.e. whether the prior art rendered other types of products containing perfluoropropane unpatentable. This is what should occur now, as well.

Election of a species for the purpose of examination is done for convenience of examination, to provide the examiner with a focus. In that practice, a part, and only a part of what is claimed, is examined initially. If that claim is not found unpatentable over the art, the examiner should proceed to examine additional aspects of what the claim covers.

Rejection of a claim under 35 U.S.C. 112 for lack of support in the specification should be done on the basis of the text of the claim as a whole, and not on the basis of an election of species. It could have been proper for the examiner to reject a claim to that specific

combination (e.g., claim 31, which has now been canceled), although, as stated above, that claim is deemed to be patentable on the basis of Dr. Hilpert's declarations.

However, rejection of claims 30, 36 and 37 (the remaining claims currently under examination) on that basis is inappropriate. Those claims are broader and define inventions beyond the combination of perfluoropropane with human protein. Claim 30, for instance, contains no requirement of an ingredient other the perfluoropropane. Claim 36 calls for a composition containing perfluoropropane that is of one of four known types of products, selected from a slightly larger number in the specification. Claim 37 calls for a composition that contains one of three gases shown in the specification to be preferred that is one of these four types of products. These claims clearly meet the written description requirement, and that is further supported by Dr. Hilpert's Fourth declaration, which provides the factual basis.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Joel G. Ackerman
Reg. No. 24,307

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
JA
SF 1252427 v1